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A Review Article On Novel Concepts Regarding Diabetes And End-Stage Renal Disease.

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ABSTRACT :

End-stage renal disease (ESRD) is most commonly caused by diabetic nephropathy, either by itself or in combination with hypertensive nephropathy in both developed and developing countries. Manuscripts published in both Persian and English, as well as full-text articles and abstracts, are included in the study. Patient survival for diabetics getting maintenance renal replacement therapy—which includes hemodialysis (HD), peritoneal dialysis (PD), and kidney transplantation—is significantly worse than for non-diabetics with end-stage renal disease (ESRD). End-stage renal disease (ESRD) patients with diabetes have a poor prognosis due in part to significant cardiovascular disease, problems with vascular access, increased vulnerability to infections, foot ulcers, and hemodynamic instability during HD.

Though many complications related to kidney transplantation may occur in diabetic ESRD patients, numerous studies have found that kidney transplantation is the preferred renal replacement therapy for diabetic patients with ESRD and is associated with a significantly better survival and quality of life than dialysis among these patients.

Keywords: hemodialysis, renal replacement therapy, diabetic nephropathy, and end-stage renal disease.

Introduction :

Proteinuria is the classic marker of diabetic nephropathy, which is seen in a significant proportion of patients with type 1, also known as insulin-dependent diabetes mellitus, and type 2, previously known as non-insulin-dependent diabetes mellitus (DM). If diabetes has been established for a sufficient amount of time and the blood sugar level is high enough to result in diabetic complications, it can also happen to people with secondary types of diabetes, such as those who have had pancreatitis or a pancreatectomy [(1,2)].

Twenty percent to thirty percent of people with type 1 DM may get microalbuminuria after an average of fifteen years; fewer than half of these patients will experience macroalbuminuria, also referred to as overt nephropathy (3-5). The development of end-stage renal disease (ESRD) is a common outcome for individuals who have overt nephropathy; rates of development vary from 4% to 17% after 20 years and approximately 16% at 30 years after the original diagnosis of DM [(1,2).] Even if the two forms of diabetes had different times to proteinuria from the beginning of the disease and to ESRD from the beginning of the disease, the times to prevalence of progressive renal disease is generally lower estimated in type 2 diabetes. Recent data, however, suggest that the renal risk is currently equivalent [(2,3)].

Angiotensin converting enzyme inhibitors (ACEI) and angiotensin II receptor blockers (ARB) are two examples of drugs that can be used in conjunction with blood pressure normalization to delay the onset and progression of diabetic nephropathy. Other agents that can be used include spironolactone and aldosterone antagonists, the non-selective phosphodiesterase inhibitor pentoxifylline, and strict control of plasma glucose concentration. Still, a considerable number of individuals experience the progression of end-stage renal disease (ESRD) [(4-6)]. The global public health concern of ESRD, however, puts a significant financial burden on healthcare systems. [(7,8)]

Methods And Materials :

To compile a range of sources for this research, we searched PubMed, Embase, Scopus, Current Content, and Iran Medex between January 1990 and December 2014.Search terms and/or synonyms used in the combination were "diabetic nephropathy" together with "end stage renal disease, ESRD, hemodialysis," "dialysis," "peritoneal dialysis," and "kidney transplantation." Manuscripts published as full-text papers, abstracts, or in both Persian and English are included in the study. Unfortunately, we did not perform a thorough hand search of conference proceedings or publications that were published in other languages.

Diabetes as an ESRD cause:

Several studies have been carried out to determine the underlying causes of ESRD in industrialized countries. For many years, the most frequent cause of end-stage renal disease (ESRD) in these nations has been glomerulonephritis (GN), in its different forms. Nonetheless, it is widely recognized that, as a result of more aggressive GN treatment and perhaps the quick rise in the prevalence of obesity and diabetes, diabetic nephropathy is currently the most common cause of end-stage renal disease (ESRD) in developed nations, either by itself or in combination with hypertensive NB. According to the United States Renal Data System, for example, diabetes accounts for approximately 45% of cases of end-stage renal disease (ESRD) and is the most common cause [9–11].

There has also been an increase in prevalence in European countries; data indicate that 34% and 29.5% of patients in Germany and Australia, respectively, requiring renal replacement therapy had diabetes [11, 12]. However, the number of Danish patients with diabetes-related end-stage renal disease (ESRD) seems to have stabilized. This could be due to the widespread adoption of strict renoprotective measures, such as improved blood pressure and glucose control[12].

It appears that diabetes and hypertension are the main causes of end-stage renal disease (ESRD) in industrialized countries as well, which is consistent with the devastating effects of these two silent killers [13–16]. Information regarding the genesis of ESRD in poor countries is scarce.

For example, the proportion of newly diagnosed patients in Iran who required renal replacement therapy increased by twofold between 1997 and 2006 [15]. This increase was associated with diabetic nephropathy. Another study conducted in Iran found that nearly 35% of cases of end-stage renal disease (ESRD) in people 40 years of age and older were caused by diabetes mellitus (DM). Additionally, hypertensive nephrosclerosis and diabetic nephropathy together account for 56% of cases of end-stage renal disease (ESRD) [13].

Other studies carried out in developing countries have shown that diabetic nephropathy is a significant contributing factor to a significant number of end-stage renal disease (ESRD) patients [17–19]. For example, Al Wakeel et al. [17] reported that in Saudi Arabia, diabetes mellitus (DM) is the most common cause of end-stage renal disease (ESRD), accounting for 26.6% of cases, followed by nephrosclerosis. It was also the most common comorbidity during the study period, occurring in 59% of cases, and heart disease in 33.7% [17]. Other Arab countries have also reported high prevalence rates of diabetes, Kuwait (21.3%), Egypt (37%), and Lebanon (46.7%) [18–20].

Diabetes Patient's Survival with ESRD :

Numerous investigations have shown that diabetic ESRD patients have poor outcomes [24–26]. For instance, the 2009 United States Renal Data System (USRDS) study states that the five-year survival rate for diabetic individuals with end-stage renal disease (ESRD) is just thirty percent following the start of HD. Comparatively, in the United States, the 1, 3, 5, and 10-year survival rates of ESRD patients receiving maintenance HD are 79%, 53%, 35%, and 11.2%, respectively. These figures are likewise significantly lower than those of the general population, where the estimated remaining life expectancy for people in the 40–45 age group is 30–39 years, and for people in the 60–67 age range is 17–20 years [27].

The study by Chantrel et al. also revealed that, even in wealthy nations with comparatively high survival rates, diabetic individuals with end-stage renal disease (ESRD) had a bad prognosis. The study conducted at a French facility found that after an average follow-up of 211 days, 32% of patients with type 2 diabetes who needed dialysis passed away [27].

While wealthy countries have conducted numerous research on the lifespan of diabetic ESRD patients receiving maintenance dialysis, there is a dearth of data from poor nations.

The two Iranian findings state that diabetic dialysis patients have a catastrophic long-term survival rate that is lower than that of non-diabetic ESRD patients [22,25,27]. The first study assessed the survival of 185 patients with end-stage renal disease on intermittent HD. While the one-year survival rate for diabetes patients is roughly the same as that of non-diabetic patients, the three- and five-year survival rates are substantially lower for diabetic patients (52.2% vs. 73.8%), and none of them had a five-year survival rate (0% vs. 56.9%) [22]. The other study looked into the long-term survival of 1861 ESRD patients in a multicenter HD in southwest Iran. Patients with diabetes had a far poorer survival rate than patients without the disease; the 1, 5, 10, and 15-year survival rates for diabetic and non-diabetic individuals are 79.2 vs.

In conclusion, diabetic dialysis patients have a poorer survival rate than non-diabetic patients based on the findings of the studies mentioned above. Now, there's a crucial query. Are the survival rates of dialysis patients with DM as the primary cause of ESRD and those with DM as a co-occurring condition different?

This issue has not been compared in many studies involving dialysis patients. Using data from the European Renal Association-European Dialysis and Transplant Association Registry, Schroijen et al. [28] compared the survival of 15,419 dialysis patients in a large multinational cohort study. Of them, 11,93 had diabetes as a comorbid condition, 10,602 did not have diabetes, and 3624 had diabetes as their primary renal disease. The results of the study show that compared to individuals without diabetes, both groups of diabetic dialysis patients had worse survival rates. Even when age, sex, location, and malignancy are taken into account, dialysis patients with diabetes as their primary renal disease had a lower survival rate than those with diabetes as a comorbid condition. Many factors are involved.

Dialysis Mode of Diabetes:

Many factors that also affect non-diabetics influence the choice of dialysis modality for diabetics, such as HD, automated peritoneal dialysis (APD), or chronic ambulatory peritoneal dialysis (CAPD). Availability and convenience, coexisting conditions, socioeconomic and dialysis center factors, patient

independence and motivation, capacity to withstand volume shifts, risk and history of infection, condition of the abdomen for Parkinson's disease (PD), and state of the peripheral vasculature to create adequate vascular access for HD are a few of them [29–39].

Patients with diabetes Patients, especially those in their later years, are more prone to suffer from severe peripheral vascular disease, which makes it more difficult to establish and maintain a sufficient arteriovenous fistula for chronic HD. Furthermore, a large number of diabetic patients also have autonomic neuropathy, which makes them more likely to experience numerous hypotensive episodes during HD, particularly during ultrafiltration dialysis when the main objective is fluid removal. Intradialytic hypotension typically requires IV fluid replacement therapy, which puts these patients at risk for volume overload. Conversely, hypotensive episodes during HD typically require a reduction in blood flow rate and, in certain cases, the cessation of HD. As a result, these patients may experience inadequate dialysis and other serious complications [33–39].

In conclusion, people with diabetes can benefit from both PD and HD treatments in a way that maximizes their respective benefits. However, given the aforementioned complication, it might be recommended that diabetic dialysis patients start off on PD then switch to HD if PD causes problems. This is partially predicated on the idea that, in contrast to HD, PD would offer superior short-term survival and preservation of residual renal function. The survival benefit associated with Parkinson's disease (PD) is temporary and occurs within the first few years of dialysis treatment, according to research using data from the United States Renal Data Systems (USRDS) and other studies [30, 34].

Digestion Compared to Kidney Transplantation:

Diabetic ESRD patients may have numerous kidney transplant-related problems. Diabetes patients have a higher frequency of cardiovascular illness than non-diabetic transplant recipients, and throughout the early and late posttransplant periods, they experience the highest rates of adverse cardiac events. Furthermore, compared to non-diabetic transplant recipients, diabetic transplant recipients are more likely to experience bacterial and fungal infections, including posttransplant urinary tract infections. After transplantation, glucose control is another difficulty for diabetic ESRD patients. Glycemic control and achieving target glucose levels are frequently more difficult after transplantation due to immunosuppressive regimens used after transplantation and their detrimental effects on pancreatic beta cell function and peripheral insulin action. As a result, the transplanted patient's risk of the diabetic lesions recurring is increased.

Several studies have revealed that kidney transplantation is the recommended renal replacement therapy for diabetic individuals with end-stage renal disease (ESRD), despite the difficulties and consequences mentioned above. These studies' findings indicate that kidney transplantation is typically linked to a significantly higher survival and quality of life for these patients than dialysis [41, 42]. For instance, survival research utilizing USRDS data revealed that diabetes transplant recipients have far higher long-term survival than dialysis patients, even if they have a significantly higher short-term mortality after surgery. Compared to the approximately 15,000 diabetics on the transplant waiting list, the 7200 diabetic transplant patients had a 73% lower risk of death 18 months after transplantation (relative risk: 0.27, 95% CI: 0.24-0.30).

Similar results were obtained from a survival analysis of 1732 individuals waiting for their first kidney transplant in Scotland, according to another study. Approximately 250 diabetic patients who had transplants had a lower risk of mortality and a much higher anticipated gain in life at 12 months after the procedure than diabetics who continued on dialysis [41].

It is hypothesized that, in part, a decline in the risk of fatal and nonfatal cardiovascular problems, particularly among diabetic patients, accounts for the mortality reduction among dialysis patients who received kidney transplantation as compared with patients who continue on dialysis [44].

Preemptive kidney replacement surgery:

Preemptive kidney transplantation is advised if at all possible rather than transplantation after a period of dialysis, as the available evidence suggests that all patients with chronic kidney disease (CKD) have a survival advantage with preemptive transplantation (before dialysis is required) when compared with initiation of dialysis followed by transplantation [45,46].

Preemptive kidney transplantation appears to be preferable among diabetic patients with chronic kidney disease (CKD) as opposed to starting dialysis first and then getting a transplant; this approach is also linked to significant increases in patient survival. For instance, the USRDS report states that among 73, 103 patients—including nearly 20,000 diabetic patients—there is an increased risk of death following transplantation of 21%, 28%, 41%, 53%, and 72% in comparison to preemptive transplants. These patients had waiting times of 6 to 12 months, 12 to 24 months, 24 to 36, 36 to 48, and more than 48 months, respectively. Moreover, longer dialysis sessions are linked to a higher risk of graft loss in all ESRD patients, including those with diabetes [45].

Based on the findings of recent research, it is unclear if using living or deceased donor kidneys will improve patient and allograft survival in preemptive transplantation among ESRD diabetic patients. For instance, preemptive kidney transplantation is linked to improved patient and allograft survival among both living and deceased donors, according to the findings of the Meier-Kriesche et al.[45] study. This study's findings are at odds with a retrospective study by Becker et al.[46] that examined over 20,000 diabetes patients and found that living donor recipients were the only ones who benefited from preemptive transplantation. This study shows that preemptive kidney transplantation from living donors reduces mortality in ESRD diabetic individuals

In summary:

Individuals with type 1 and type 2 diabetes have a notable proportion of individuals with diabetic renal damage. While type 2 diabetes is traditionally associated with a lower prevalence of progressive renal disease, recent data indicate that the two forms of diabetes have similar times to end-stage renal disease (ESRD) from the beginning of proteinuria and an equivalent renal risk at now. The devastating aftereffects of these two silent killers are well

known to indicate that diabetic nephropathy, especially type 2, and hypertension nephropathy are the main causes of end-stage renal disease (ESRD) in both industrialized and developing nations.

Among comparison to non-diabetics with ESRD, patient survival is poorer among diabetics receiving continuous dialysis, including HD and PD. Compared to individuals with diabetes as a comorbid condition, it appears that dialysis patients with diabetes as the primary renal disease have a poorer survival rate.

PD or HD can be used to treat diabetic people. It might be recommended that diabetic dialysis patients get PD at first since it helps to better preserve their remaining renal function and improves their short-term survival. Nevertheless, numerous studies' analyses have revealed that the longevity advantage linked to Parkinson's disease (PD) is only present in the initial years of dialysis and gradually disappears.

Numerous studies have found that kidney transplantation is the preferred renal replacement therapy for diabetic patients with ESRD and is associated with a significantly better survival and quality of life than dialysis among these patients, despite the fact that many complications related to kidney transplantation may occur in diabetic ESRD patients.

The available data suggests that diabetic patients with CKD, like other CKD patients, have a survival advantage with preemptive transplantation when compared with starting dialysis followed by transplantation. Therefore, if at all possible, preemptive transplantation is advised rather than transplantation after a dialysis period. However, whether utilizing kidneys from living or deceased donors enhances allograft and patient survival in patients with end-stage renal disease undergoing preventive transplantation is unknown.

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